

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-711

ADMINISTRATIVE DOCUMENTS

CSO Review of Labeling

NDA 20-711

**Drug: Zyban (bupropion hydrochloride) SR Tablets for smoking cessation,
100 mg and 150 mg**

Sponsor: Glaxo Wellcome Inc.

Materials Reviewed:

Draft labeling submitted with the NDA application on May 17, 1996; labeling amendments of October 3, November 8, 1996, February 14, 21, March 25, April 18, 23, 28, and May 1, 1997.

Review: The labels are in conformity with labeling regulations (21 CFR 201.1, 201.5, 201.10, 201.15, 201.17, 201.18, 201.50, 201.51, 201.55, and 201.100).

Conclusions:

Draft versions of the container labeling ^{in 1996} was submitted on May 17, 1996 and February 21, 1997. The version submitted in February was approved by the chemistry reviewer and is located in the NDA action package under Approved Labeling - Container Labels Approved.

Draft versions of the patient package insert were submitted on May 17 and October 3, 1996. The division held labeling meetings on October 8, and October 11, 1996. The division's edited label was faxed to the sponsor on October 18, 1996. The division held another meeting on October 25, 1996 and faxed changes to the sponsor on October 29, 1996. The sponsor submitted revised labeling on November 8, 1996. The division met to revise this version on November 14, 1996. This revised version was finalized on November 15, 1996 and was included in a package of pre-meeting materials to the Drug Abuse Advisory Committee members. This version was also faxed to the sponsor. The sponsor submitted a new revision on February 14, 1997. The division met to edit this on March 13, 1997. The changes were faxed to the sponsor on March 18, 1997. On March 19, the sponsor faxed comments on the package insert and a telecon was held with the sponsor to discuss it. On March 25, 1997, the sponsor submitted revised "Patient Information" and "How Supplied" sections to the division. Medical officers of the division made revisions to the March 25th submission and another telecon was held with the sponsor on ~~on~~ April 2, 1997. The agreed upon changes were incorporated into the 4/2/97 version which was submitted to HFD-120 to see if this version was consistent with their package insert for Wellbutrin SR (This is exactly the same formulation as Zyban). Dr. Leber, of HFD-120, sent a memo to the division on April 22, 1997 with a note stating some concerns and also indicating that HFD-120 had no objections to the label as written. Dr. Winchell wrote a response to HFD-120's concerns on May 1, 1997. (This version also went to Dr. Botstein for review, but she ultimately ~~reviewed~~ returned this version and reviewed a later version.) This version was faxed to the sponsor on April 4,

1997. On April 14, 1997, the division faxed some suggested changes from DDMAC to the sponsor. The sponsor submitted another revision on April 18, 1997. A review of this was prepared by the medical reviewer on April 29, 1997 and faxed to the sponsor. On May 1, 1997, the sponsor submitted another revision. This version was cleared by the medical reviewer and submitted to Dr. Botstein for review on May 5, 1997. On March 14, 1997 a meeting was held with Dr. Botstein and final changes were made to the label.

The ancillary materials were considered labeling and reviewed by the medical staff. The draft materials were submitted on February 21 and April 18, 1997. All materials submitted on April 18, 1997 were approved except the Patient's Program Guide and the Zyban Q & A. The latter were submitted and approved on May 1, 1997.

Concur: Corinne P. Moody
Corinne P. Moody
Chief, Project Management Staff

Bonnie McNeal 8/22/97
Bonnie McNeal
Project Manager

cc:

Orig NDA 20-711

Div File

HFD-170/BMcNeal/Moody

PEDIATRIC PAGE
(Complete for all original applications and all efficacy supplements)

NDA # 20-711

Supplement # -----

Circle one: SE1 SE2 SE3 SE4 SE5 SE6

HFD-170 Trade and generic names/dosage form: Zyban (bupropion hydrochloride sustained release tablets),
100 mg and 150 mg

Action: AP AE NA

Applicant: Glaxo Wellcome Inc.

Therapeutic Class: Smoking cessation product

Indication(s) previously approved: same active ingredient approved for treatment of depression

Pediatric information in labeling of approved indication(s) is adequate inadequate *N/A see attached memo.*

Indication in this application: as an aid to smoking cessation treatment

(For supplements, answer the following questions in relation to the proposed indication.)

1. PEDIATRIC LABELING IS ADEQUATE FOR ALL PEDIATRIC AGE GROUPS. Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for all pediatric age groups. Further information is not required.

2. PEDIATRIC LABELING IS ADEQUATE FOR CERTAIN AGE GROUPS. Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for certain pediatric age groups (e.g., infants, children, and adolescents but not neonates). Further information is not required.

3. PEDIATRIC STUDIES ARE NEEDED. There is potential for use in children, and further information is required to permit adequate labeling for this use.

a. A new dosing formulation is needed, and applicant has agreed to provide the appropriate formulation.

b. A new dosing formulation is needed, however the sponsor is either not willing to provide it or is in negotiations with FDA.

c. The applicant has committed to doing such studies as will be required.

(1) Studies are ongoing,

(2) Protocols were submitted and approved.

(3) Protocols were submitted and are under review.

(4) If no protocol has been submitted, attach memo describing status of discussions.

d. If the sponsor is not willing to do pediatric studies, attach copies of FDA's written request that such studies be done and of the sponsor's written response to that request.

4. PEDIATRIC STUDIES ARE NOT NEEDED. The drug/biologic product has little potential for use in pediatric patients. Attach memo explaining why pediatric studies are not needed. *see attached memo.*

5. If none of the above apply, attach an explanation, as necessary.

ATTACH AN EXPLANATION FOR ANY OF THE FOREGOING ITEMS, AS NECESSARY.

Bonnie McNeal / Project Manager

April 28, 1997

Signature of Preparer and Title

Date

cc: Orig NDA # 20-711
HFD-170 /Div File
NDA Action Package
HFD-006/ SOlmstead (plus, for CDER/CBER APs and AEs, copy of action letter and labeling)

NOTE: A new Pediatric Page must be completed at the time of each action even though one was prepared at the time of the last action. (revised)

REQUEST FOR TRADEMARK REVIEW

To: Labeling and Nomenclature Committee
Attention: Dan Boring, Chair (HFD-530) NLRC

From: Division of Anesthetic, Critical Care and Addiction Drug Products	HFD-170
Attention: Bonnie McNeal	Phone: 443-3741
Date: November 25, 1996	
Subject: Request for Assessment of a Trademark for a Proposed New Drug Product	
Proposed Trademark: QUITAB	NDA 20-711
Established name, including dosage form: Bupropion Hydrochloride Sustained Release Tablets 50 mg, 100mg and 150 mg	
Other trademarks by the same firm for companion products: Wellbutrin SR is indicated to treat depression. It is exactly the same dosage form as this NDA. Wellbutrin SR is NDA 20-358. The sponsor is Glaxo Wellcome.	
Indications for Use (may be a summary if proposed statement is lengthy): As an aid to smoking cessation	
Initial Comments from the submitter (concerns, observations, etc.): The Drug Abuse Advisory Committee will consider the question of the safety of marketing under two tradenames. (The committee meets on December 12, 1996.) We are the asking the Nomenclature Committee for comment on the appropriateness of the specific name. We have no comments about the sponsor's choice of a tradename.	

Note: Meetings of the Committee are scheduled for the 4th Tuesday of the month. Please submit this form at least one week ahead of the meeting. Responses will be as timely as possible.

Rev. August 95

United States Patent [19]

[11] E

Patent Number: Re. 33,994

Baker et al.

[45] Reissued Date of Patent: Jul. 14, 1992

[54] PHARMACEUTICAL DELIVERY SYSTEM

1326995 8/1973 United Kingdom
2025227 1/1980 United Kingdom

[75] Inventors: Richard W. Baker, Palo Alto, Calif.;
James W. Brooke, Sisters, Oreg.

[73] Assignee: Burroughs Wellcome Co., Research
Triangle Park, N.C.

[21] Appl. No.: 390,518

[22] Filed: Aug. 4, 1989

OTHER PUBLICATIONS

Wellbutrin: Comprehensive Bibliography of Published
Literature Nov. 13, 1989, pp. 1-91.

Webster's New Collegiate Dictionary, G. & C. Merriam
Co., Springfield, Mass., U.S.A. 1956, p. 3.

Asol & Hoover "Remington's Pharmaceutical Sci-
ences," 15th edition, 1975, Mack Publishing Company,
Easton, Pa., pp. 1608-1617.

Lieberman & Lachman "Pharmaceutical Dosage
Forms: Tablets", vol. 3, 1982, Marcel Dekker, Inc.
N.Y., N.Y., pp. 73-117.

Webster's New International Dictionary of the English
Language, 2nd edition, Unabridged, G & C Merriam
Company, Springfield, Mass., 1939, p. 2540.

Webster's Third New International Dictionary of the
English Language Unabridged, G & C Merriam Com-
pany, Springfield, Mass., 1963, p. 2302.

Journal of Pharmaceutical Sciences, Jul. 1983, vol. 72,
No. 7, pp. 772-775.

Primary Examiner—Ronald W. Griffin
Attorney, Agent, or Firm—Donald Brown; Lawrence A.
Nielsen

Related U.S. Patent Documents

Reissue of:

[64] Patent No.: 4,687,660
Issued: Aug. 18, 1987
Appl. No.: 640,951
Filed: Aug. 15, 1984

[30] Foreign Application Priority Data

Aug. 16, 1983 [GB] United Kingdom _____ 8322007

[51] Int. Cl.⁵ _____ A61K 9/22; A61K 9/32;
A61K 31/60

[52] U.S. Cl. _____ 424/465; 604/890.1;
604/892.1; 514/964; 424/473; 424/468;
424/469

[58] Field of Search _____ 424/465, 473, 468, 469;
514/964; 604/890, 892, 893

References Cited

U.S. PATENT DOCUMENTS

2,011,587	8/1935	Miller	424/465
2,987,445	6/1961	Levesque	424/465
3,143,463	8/1964	Holm et al.	514/654
3,146,169	8/1964	Stephenson et al.	424/467
3,538,214	11/1970	Polli et al.	424/473
3,773,920	11/1973	Nakamoto et al.	424/465
3,819,706	6/1974	Mehta et al.	514/649
3,885,046	5/1975	Mehta	514/649

(List continued on next page.)

FOREIGN PATENT DOCUMENTS

280478	4/1970	Austria
305498	2/1973	Austria
0086093	8/1983	European Pat. Off.
0111144	6/1984	European Pat. Off.
0159604	10/1985	European Pat. Off.

[57] ABSTRACT

A composition for use in an aqueous environment
which [comprise] comprises a formulation containing
a water-soluble pharmaceutically beneficial agent, a
water-insoluble, water-permeable film coating sur-
rounding the formulation, and particulate, water-solu-
ble, pore-forming material dispersed within the film
coating.

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The questions raised in reexamination request No.
90/001,344, filed Oct. 5, 1987, have been considered and
the results thereof are reflected in this reissue patent
which constitutes the reexamination certificate required
by 35 U.S.C. 307 as provided in 37 CFR 1.570(e).

1 Claim, 1 Drawing Sheet

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4,256,108	3/1981	Theeuwes _____	604/893	4,439,196	3/1984	Higuchi _____	604/890
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4,327,725	5/1982	Cortese et al. _____	604/893	4,519,801	5/1985	Edgren _____	604/890
4,347,176	8/1982	Mehta _____	530/363	4,539,198	9/1985	Powell et al. _____	424/465
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4,347,257	8/1982	Stern _____	514/649	4,687,660	8/1987	Baker et al. _____	424/465
4,347,382	8/1982	Scharver _____	564/183	4,769,027	9/1988	Baker et al. _____	424/493
				4,798,826	1/1989	Peck _____	514/221

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3,819,706

META CHLORO SUBSTITUTED- α -BUTYLAMINO-PROPIOPHENONES

Nariman B. Mehta, Raleigh, N.C., assignor to Burroughs Wellcome Co., Research Triangle Park, N.C.

No Drawing. Filed Nov. 30, 1970. Ser. No. 93,852

Claims priority, application Great Britain, Dec. 4, 1969, 59,231/69

Int. Cl. C07c 97/10

U.S. Cl. 260—570.5 C

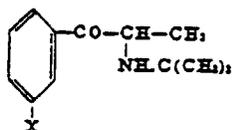
6 Claims

ABSTRACT OF THE DISCLOSURE

The compounds *m*-chloro- α -*t*-butylaminopropiophenone and *m*-fluoro- α -*t*-butylaminopropiophenone or salts thereof. The compounds are useful in the treatment of mammals suffering from a depressed state.

The present invention relates to α -alkylaminopropiophenones.

It has been found that the two novel compounds represented by the general formula (I)

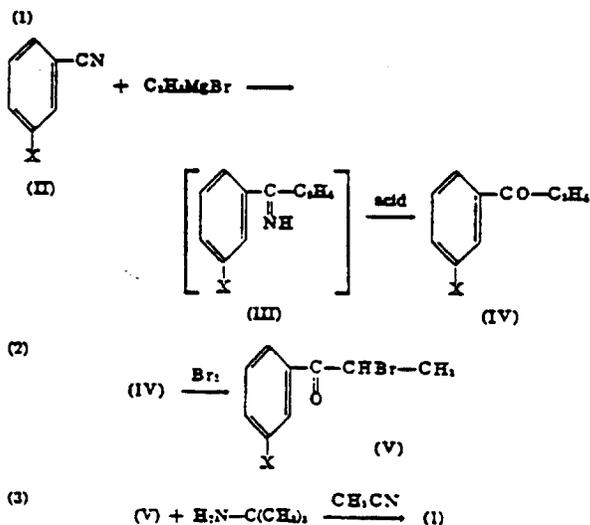


and acid addition salts thereof, in which X is chlorine or fluorine, possess valuable properties as antidepressants when tested by standard techniques used in the art for determining antidepressant activity, for example the tetra-benzazine-induced sedation test in rodents. It has been found specifically that the compounds of formula (I) require much larger doses for stimulant action than for antidepressant action. The compounds are also not inhibitors of mono-amine oxidase, nor do they have a pressor effect.

Closely related alkylaminopropiophenones are already known and have been proposed for various pharmaceutical purposes; see for example British Patent Specifications 768,772; 1,011,289; and 1,069,797. The activity of the two novel compounds of the present invention appears to be outstanding and not possessed by related known compounds.

The compounds may be synthesised by the methods known in the art for this type of compound.

A particularly convenient route is that set out in the following reaction scheme:



The propiophenones, (IV), are not commercially available, and Step (1) has been found a convenient method of preparation. The bromination Step (2), is not very rapid and may require heating. It is not necessary to isolate the ketone (V) as a pure substance provided the hydrogen bromide produced in Step (2) is removed.

It will of course be understood that in Step (3) above, the *m*-X- α -bromopropiophenone (V) may be replaced by the corresponding α -chloro- or α -iodo-compounds. *m*-X- α -Chloropropiophenones may be prepared conveniently by reaction of *m*-X-propiophenone with sulphuryl chloride. The *m*- α -dichloropropiophenone may also be conveniently prepared from α -chloropropiophenone by reaction with sulphuryl chloride in the presence of aluminium chloride. The reaction of Step (3) is subject to hindrance and *t*-butylamine normally reacts very slowly with α -bromopropiophenones. It is desirable to include an organic solvent in the reaction mixture, and for this purpose acetonitrile offers marked advantages. It is a "fast" solvent, is unreactive under the conditions and is relatively low boiling. Other polar solvents, protic or aprotic, may be used, for example lower aliphatic ketones or ethers, but the reaction is slow in these solvents. Others which may be used include dimethylformamide, nitromethane, dimethylsulphoxide and hexamethylphosphoramide.

It is desirable to heat the reactants of Step (3), for example at the reflux temperature of the reaction mixture. The amine is preferably present in excess relative to the ketone; up to five times the equimolar quantity may be used. If the ketone is a *m*-X- α -chloropropiophenone, then a catalytic amount of an iodide salt, for example sodium iodide, may be included in the reaction mixture.

Once isolated the *m*-X- α -*t*-butylaminopropiophenones of formula (I) are stable and can be distilled *in vacuo* although this is not normally necessary. They are moderately weak bases (pKa around 8.5-9) and are desirably stored and administered as a pharmaceutically acceptable salt, conveniently one of a mineral acid such as the hydrochloride salt. Under physiological conditions, they would be predominantly (but not exclusively) cationic. In any case, if administered as one salt, they would be in equilibrium with the various anions corresponding to other acids present in the body and their salts with different acids can possess advantages only in convenience of isolation or solubility not in inherent physiological behaviour. Accordingly, it is considered that all salts of the bases of formula (I) with non-toxic acids are equivalent to each other and to the bases.

It will be readily understood that salts of acids which are not pharmaceutically acceptable may also have value as intermediates for the preparation of the acceptable salts by double decomposition, base exchange and other well known methods.

According to the present invention there is provided a compound of the formula (I) and a pharmaceutically acceptable salt thereof.

According to the present invention, in yet another aspect, there is provided a pharmaceutical composition (preferably in unit dosage form) comprising a compound of formula (I) (or a pharmaceutically acceptable salt thereof) together with a pharmaceutically acceptable carrier. Conveniently the compound of formula (I) or its acid addition salt comprises from 5 to 95% by weight of the composition.

According to the present invention in yet another aspect there are provided methods of synthesising compounds of formula (I) comprising the application of analogous methods specified above for the preparation of alkylaminopropiophenones.

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According to still a further aspect of the present invention, there is provided a method of treating a depressed state in mammals such as humans, mice, rats, etc., which comprises the administration of an antidepressant effective non-toxic amount (dose), preferably in a unit dosage form, of a compound of formula (I) or a pharmaceutically acceptable salt thereof.

The compounds of formula (I) (the active ingredients) or the pharmaceutically acceptable salt thereof is preferably administered in unit dosage form to the mammal being treated.

The compounds of this invention may be administered orally, parenterally or rectally.

A pharmaceutical composition containing a compound of formula (I), or a pharmaceutically acceptable salt thereof, may be presented in discrete units such as tablets, capsules, ampoules or suppositories, each containing an effective antidepressant non-toxic amount of the compound.

The preferred dosage for parenteral administration of a compound of formula (I) (estimated as the base) is about 5 mg./kg. to 50 mg./kg. of mammal body weight, and the most preferred dosage being 15 mg./kg. to 35 mg./kg. of mammal body weight.

For the oral or rectal mode of administration, the preferred dosage of a compound of formula (I) (estimated as the base) is about 10 mg./kg. to 100 mg./kg. of mammal body weight while the most preferred dosage (estimated as the base) is about 30 mg./kg. to 70 mg./kg. of mammal body weight. A compound of formula (I), or an acid addition salt thereof, is preferably administered four times daily although the number of daily administrations of the medication may vary according to the patient (mammal) being treated, and the exercise of the physician's discretion.

For the treatment of humans, the preferred unit dosage of a compound of formula (I) or an acid addition salt thereof (estimated as the base) for oral administration, or administration as a suppository, is about 15 milligrams to 500 milligrams with the more preferred unit dosage being about 100 milligrams to 300 milligrams, and the most preferred unit dosage being about 125 milligrams to 250 milligrams. All the above doses are given in terms of the weight of a compound of formula (I) in the form of its base, but as will be appreciated from the foregoing information, it is preferably administered in the form of a pharmaceutically acceptable acid addition salt thereof.

A compound of formula (I) or pharmaceutically acceptable salts thereof may be presented as an oral unit preparation (for example as a cachet, tablet or capsule) containing one or more pharmaceutically acceptable carriers which may take the form of solid diluents such as lactose, cornstarch, micronized silica gel, as well as other excipients well known in the art for this purpose.

A compound of formula (I) or a pharmaceutically acceptable salt thereof may be presented for rectal use as a suppository with the usual pharmaceutically acceptable carriers such as cocoa butter, and may be presented for parenteral use as an ampoule of a sterile solution or suspension with water or other pharmaceutically acceptable liquid as the carrier therefor, or as an ampoule of a sterile powder for dilution with a pharmaceutically acceptable liquid.

It should be understood that in addition to the aforementioned ingredients, the pharmaceutical compositions of this invention may include one or more of additional ingredients such as diluents, buffers, flavouring agents, binders, surface active agents, thickeners, lubricants, preservatives, and the like. The formulations may be prepared by admixture of the ingredients, and, if necessary, shaping the resulting mass, and filling into suitable containers.

The compound of formula (I) is preferably presented for use in the treatment of depressed states as a pharmaceutically acceptable salt. Examples of some of the pharma-

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aceutically acceptable salts which can be utilized are salts of the following acids: hydrochloric, sulfuric, phosphoric and toluenesulphonic.

The invention will now be illustrated with reference to the following examples:

EXAMPLE 1

Preparation of *m*-Chloro-*α*-*t*-butylaminopropiophenone

(a) *m*-Chloropropiophenone.—To ethyl magnesium bromide (2 L; 3M) was added over 45 minutes with stirring and cooling *m*-chlorobenzonitrile (688 gm.; 5 mole) in ether (2.5 L). The resultant solution was heated under gentle reflux for 5 hours.

The reaction-mixture was hydrolyzed with cold dilute hydrochloric acid, the ether was distilled off, and the aqueous solution was heated at 90° C. for one hour. The flask was then cooled and seeded. The solid ketone that separated was washed with cold water and recrystallized from methanol. The recrystallized ketone, m.p. 39–40°, weighed 750 gm.

(b) *m*-Chloro-*α*-*t*-bromopropiophenone.—In methylene chloride (3 L) was dissolved *m*-chloropropiophenone (698 gm.; 4.15 mole). The solution was stirred with charcoal (Darco) and magnesium sulfate for two hours and filtered. To it was added with stirring 662 grams (4.15 mole—2 g.) of bromine in methylene chloride (1 L). When the bromine colour had faded completely, the solvent was evaporated *in vacuo*.

(c) *m*-Chloro-*α*-*t*-butylaminopropiophenone hydrochloride.—The oily residue obtained in the manner of paragraph (b) was dissolved in acetonitrile (1300 ml.). To this, *t*-butylamine (733 gm.) in acetonitrile (1300 ml.) was added while keeping the temperature below 32° C. The reaction mixture was allowed to stand over-night. It was then partitioned between water (4200 ml.) and ether (2700 ml.). The aqueous layer was extracted with a further portion of ether (1300 ml.). The combined ethereal layers were then washed with water (4200 ml.) to which hydrochloric acid was added until the pH of the aqueous layer was 9. The aqueous layer was separated and washed with ether (500 ml.) and then discarded. The combined ethereal layers were then stirred with ice (560 gm.) and concentrated hydrochloric acid (324 ml.). The ethereal layer was separated and again washed with water (200 ml.) and concentrated hydrochloric acid (50 ml.). These last two acid layers were combined and concentrated *in vacuo* until crystals appeared. The solution was then chilled to 5° C. and filtered. The product was sucked dry, washed with acetone and recrystallized from a mixture of isopropanol (3 L) and absolute ethanol (800 ml.). The DL-*m*-chloro-*α*-*t*-butylaminopropiophenone hydrochloride so obtained was analytically and spectrographically pure, m.p. 233–234° C.

EXAMPLE 2

Preparation of *m*-Fluoro-*α*-*t*-butylaminopropiophenone

(a) *m*-Fluoropropiophenone.—Ethyl magnesium bromide was reacted with *m*-fluorobenzonitrile by the procedure of Example 1(a). The ketone boils at 89° C. at 8 mm. pressure and melts at 29–30° C.

(b) *m*-Fluoro-*α*-*t*-butylaminopropiophenone hydrochloride.—The bromination of the product described in paragraph 2(a) was conducted as described in Example 1(b), and reaction of the *α*-bromoketone with *t*-butylamine as described in Example 1(c). The DL-aminoketone hydrochloride melted at 225–226° C.

While in the processes of Examples 1 and 2, the hydrochlorides were obtained directly without isolation of the bases, it is also feasible to separate the bases by vacuum distillation. *m*-Chloro-*α*-*t*-butylaminopropiophenone was distilled at 52° C. and 5 μ (0.005 mm.) Hg pressure. The *m*-fluoro analogue was distilled at 44–48° C. and 40 μ (0.04 mm.) Hg pressure.

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EXAMPLE 3

Tablet Formulation 300 mg. Tablet Ingredients

150 mg. of a hydrochloride salt of formula (I)
 85 mg. Lactose
 50 mg. Cornstarch
 10 mg. Micronized Silica Gel
 5 mg. Polyvinyl pyrrolidone

Procedure

The lactose, cornstarch and salt were mixed together and granulated with a binder, polyvinyl pyrrolidone in alcoholic solution, to form granules. The granules were passed through a 16-20 mesh screen, then air dried, lubricated with micronized silica gel and compressed into tablets. A film coating could then have been applied if desired.

EXAMPLE 4

Capsule Formulation 400 mg. Fill Weight

150 mg. of a hydrochloride salt of a compound of formula (I) were mixed with 125 mg. of lactose and 125 mg. of cornstarch. The mixture was filled into a two piece hard gelatin capsule.

EXAMPLE 5

Parenteral Solution

150 mg. of a hydrochloride salt of formula (I) was dissolved in sterile water U.S.P. to make 1 ml. A multi-dose preparation may include bacteriostats such as 0.2 to 0.5% w/v. of phenol.

EXAMPLE 6

Suppository of 400 mg. Weight

150 mg. of a hydrochloride salt of formula (I) were mixed with 250 mg. of softened or melted cocoa butter,

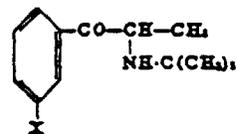
6

and suppositories were formed by chilling and shaping in moulds.

What I claim is:

1. A compound of the general formula

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or an acid addition salt thereof wherein X is chlorine.

2. A pharmaceutically acceptable acid addition salt of a compound claimed in claim 1.

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3. A mineral acid addition salt of the compound claimed in claim 1.

4. *m*-Chloro-*n*-t-butylaminopropiophenone.

5. A hydrogen halide acid addition salt of the compound claimed in claim 4.

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6. *m*-Chloro-*n*-t-butylaminopropiophenone hydrochloride.

References Cited

UNITED STATES PATENTS

25	3,313,687	4/1967	Siemer	260—570.5	X
	3,465,039	9/1969	Siemer	260—570.5	X
	2,997,472	8/1961	Janssen	260—570.5	X

FOREIGN PATENTS

30	13,215	8/1961	Japan	260—570.5
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ROBERT V. HINES, Primary Examiner

U.S. Cl. X.R.

35 260—465(G), 501.19, 566(R), 592; 424—316, 330

REQUEST FOR TRADEMARK REVIEW

To: Labeling and Nomenclature Committee
Attention: Dan Boring, Chair (HFD-530) NLRC

From: Pilot Drug Evaluation Staff		HFD-170
Attention: Bonnie McNeal		Phone: 443-3741
Date: January 21, 1997		
Subject: Request for Assessment of a Trademark for a Proposed New Drug Product		
Proposed Trademark: ZYBAN		NDA 20-711
Established name, including dosage form: Bupropion Hydrochloride Sustained release Tablets		
Other trademarks by the same firm for companion products: Wellbutrin SR for the same formulation: Wellbutrin for the immediate release formulation		
Indications for Use (may be a summary if proposed statement is lengthy): To be used as an aid for smoking cessation		
Initial Comments from the submitter (concerns, observations, etc.): The division has some concerns that a name should be chosen to fall alphabetically immediately after Wellbutrin SR in the PDR and so that physicians would be aware of two proprietary names for the same formulation. This might prevent some medication errors.		

Note: Meetings of the Committee are scheduled for the 4th Tuesday of the month. Please submit this form at least one week ahead of the meeting. Responses will be as timely as possible.

Rev. August 95

Consult #730(HFD-170)

ZYBAN

bupropion hydrochloride sustained release tablets

There were no look-alike/sound-alike conflicts or misleading aspects found in the proposed proprietary name. However, the Committee feels the appropriate established name for this product is (bupropion hydrochloride extended release tablets) to be in conformance with USP nomenclature conventions. The USP no longer uses the term "sustained release" as a dosage form descriptor.

The Committee has no reason to find the proposed proprietary name unacceptable.

D. U. Boring 3/4/97, Chair
CDER Labeling and Nomenclature Committee

cc: Orig NDA 20-711
D.V. File

HFD-170 / P. Maturin / B. Munkal